Concomitant Cisplating and Radiationtherapy in Advanced Head and Neck Cancers:

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Abstract :

Single modality treatment is not suitable to the treatment of Head and Neck cancers and surgery is often mutilating. Concomitant chemotherapy and radiation produce good local control. In this study cisplating given concomitantly with radiation is compared with radiation alone in advanced head and neck cancers.

INTRODUCTION

The management of advanced Head and Neck malignancy continues to pose a challenging problem to Head and Neck Surgeons and Oncologists.

Most Head and Neck cancers are traditionally treated with some form of surgery or followed by radio therapy. Results of treatment of these tumors are inversely proportional to the extent of the disease with the complete response being only 33% for T4N3 tumors with radiotherapy alone (Marcial 1990). Even if surgery and radiotherapy are combined local tumor control remains a significant problem with local or regional recurrence in upto 50% of cases. Only a small percentage can be salvaged with further surgery or radiation. The unfavourable results combined with the functional and cosmetic disabilities associated with treatment and or local tumor recurrence, have led to the investigation of the addition of chemotherapy to combined modality programmes for those patients at high risk for recurrence (Clark 1991).

The chemotherapeutic agents that have been used extensively in these tumors are Methotrexate, Hydroxyures and Bleomycin (Hamner III).

Cisplatin, both as a single agent and in combination with 5-fluoro uracil is active against squamous cell carcinoma in Head and Neck and may be superior to methotrexate in anti tumor activity. The impact of induction and adjuvant chemotherapy or concurrent chemotherapy and radiotherapy in patients with potentially curable lesions remains controversial.

Several phase I-II studies have been conducted in which Cisplatin has been used concomitantly with radiotherapy (Leipzig, Wheeler 1988). It was felt that in view of the findings in these studies, a prospective randomized trial was justified. In the present study Cisplatin is being used as a single agent in a concurrent regimen with radiation therapy.

Materials and Methods:

All the patients attending the Radiotherapy

department between October 1990 and May 1991 having advanced squamous cell carcinoma of the Head and Neck were included in the study.

Selection Criterial:

1. Patient should have locally advanced squamous cell carcinoma of the Larynx, oropharynx or hypopharynx.
2. Disease should be biopsy proven.
3. Patient should not have had any previous treatment.
4. Patients should be below the age of 60 years.
5. Karnofsky's performance status of the patient should be less than or equal to 60%.
6. Additional eligibility criteria were a Hemoglobin of more than or equal to 10g%, Total WBC count of more than or equal to 3000/mm³, platelet count of more than or equal to 1,00,000/mm³, serum creatinine of less than or equal to 1.5 mg% and serum Alkaline phosphatase of less than or equal to 120u/l.
7. There should be no evidence of distant metastases as evidenced clinically and by chest X-ray.
8. All patients should give informed consent.

Randomization:

The cases, after pre-treatment evaluation were randomized into two groups. Randomization was done using the closed envelope method.

Patients receiving Radiotherapy and concomitant chemotherapy were included in Group I and those receiving only Radiotherapy were in Group II.

Radiation Therapy :

External radiotherapy was given to the primary tumor by parallel opposed lateral fields upto a dose of 60gy. An additional lower neck field

was added in most cases to cover the lower neck nodes.

Patients underwent weekly check-ups while on radiation therapy to assess skin and mucosal reaction.

Chemotherapy:

Inj. Cisplatin 100 mg was administered concurrently on Days 0, 21 and 43 of radiation therapy.

Follow - up:

Patient were to be evaluated for response to treatment at 6 weeks, 3 months and 6 months.

At the follow-up, they were assessed for regression of the primary and secondary.

Criteria for Response :

No response	: Disease same as or regression less than 50% of pre-treatment status.
Partial regression (PR)	: Regression of more than 50% of pre-treatment status.
Complete regression (CR)	: No evidence of disease.
Progressive disease	: Disease more than that of pre-treatment status.

Results:

Twenty eight patients entered into the study between October 1990 and May 1991.

A sample size of 14 each was obtained in Groups I and II. All patients had full pre-treatment evaluation and were eligible for analysis.

Pre Treatment Characteristics:

(i) Symptomatology:

Majority of patients (21/28) had dysphagia as a symptom followed by Neck swelling (19/28),

Voice change (19/28), Ear/pain (9/28) and bleeding (5/28).

(2) Stage (UICC-TNM, 1987)

In Group I the number the patients with stage III disease were 3/14 (21.4%) and the number with stage IV were 11/14 (78.6%).

In Group II the number of patients in stage III were 4/14 (28.6%)and the number in stage IV were 10/14 (71.4%).

(3) Site:

In Group I the number of cases in the oropharynx were 6/14 (42.9%)and in Group II were 8/14 (57.1%).

In Group II the number of cases in the laryngopharynx were 8/14 (57.1%) and in Group II were 6/14 (42.9%).

(4) Histology:

In Group I the number of patients with well differentiated tumors were 3/14 (21.4%), the moderately differentiated tumors were 7/14 (50%) and the poorly differentiated tumors were 4/14 (28.6%).

In Group II the number of patients with well differentiated tumors were 3/14 (21.4%), moderately differentiated tumors were 9/14 (64.3%) and the poorly differentiated tumors were 2/14 (14.3%).

In the both groups tumors with moderate differentiation were the highest in number.

Tumor Control :

(i) Treatment vs Response

Of the twenty eight patients entered in the study one patient was lost to follow-up.

Three of the patients in Group I refused third course of chemotherapy but were included in the analysis.

One patient each in Group I and II had only 45 Gy to the primary tumor a spinal cord could not be shielded. There were also included in the analysis.

In patients receiving chemotherapy and radiotherapy the complete regression of primary disease was seen in 13 of 14 patients (92.9%) One patient (7.1%) had partial regression.

Complete regression of primary was seen in ii of 13 patients (84.6%) in patients receiving only radiation therapy.

In patients with secondaries, receiving radiation and chemotherapy 8 of the patients (66.6%) had complete regression (36.4%).

In patients with secondaries who only received radiotherapy 7 out of 13 patients (53.9%) had complete regression and 6/13 patients (46.1%) had partial regression.

Overall, when complete regression of disease was considered, 10 out of 14 patients (71.4%) had no evidence of disease and in 4 out of 14 patients (28.6%) there was partial regression of disease in patients receiving both radiotherapy and chemotherapy.

In patients receiving only radiotherapy 7 out of 13 (53.8%) patients had no evidence of disease at evaluation and 6 out of 13 (46.2%) had partial regression of disease.

A test of significance (chi-square) was done but the test cannot be used for interpretation as the numbers are small.

(2) Acute Toxicity:

The pattern of mucositis did not show any difference with four patients in each group needing a period of rest.

Discussion:

Carcinoma of the Head and Neck region is one of the most common malignancies seen in our set up. It forms about 17% of the malignancies in one year most of which present in an advanced stage.

Several phase II-III studies (Devita 1993, Williams 1979) have been conducted indicating that the combination of Cisplatin and radiotherapy is an effective and safe treatment in

patients with advanced head and neck cancer and needs to be tested against radiotherapy alone.

In this small population of patients evaluated the group given concomitant Cisplatin and radiotherapy had marginally better tumor regression but this was not statistically significant (figure 1 & 2).

Fig. 1 Advanced Oral Cancer before treatment.

Fig. 2 The same patient after chemoradiation.

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